REMARKS/ARGUMENTS

Claims 384, 386, 387, 392, 394-396 and 402 are pending in the application. Claim 384 is amended is delete the carrier protein *Chlamydia pneumoniae* ORF T367. No new matter is added.

Claims Rejections - 35 USC § 103

Claims 384, 386 and 387

Claims 384, 386 and 387 are rejected under 35 USC 103(a) as allegedly being unpatentable over **Mariotti** *et al.*, *Vaccine* 20:2229-2239 (2002) in view of WO 01/93804 to **Conley** *et al.* for the reasons set forth in the Office Action of December 30, 2009. In summary, the Examiner states that Mariotti teaches the conjugation of peptides to CRM_{197}, and that Conley teaches the capping of unreacted crosslinking agents on peptide-OMPC conjugates.

The Examiner dismisses Applicants arguments of June 30, 2010 as irrelevant, stating that Conley does not need to discuss maintaining immunogenicity by capping unreacted crosslinking agents because three of the five peptidyl conjugates presented in Figure 3 (presumably the Examiner meant Table 3) maintained significant immunogenicity, and that a skilled artisan would have recognized the desirability of capping to prevent unwanted reactions, such as multimerization of conjugates. *See* p. 4, 1st paragraph of the Office Action (OA).

Applicants respectfully traverse and submit that the Examiner may have misunderstood Applicants' argument of June 30, 2010. Applicants do not dispute that the capped conjugates exemplified in Conley (in Table 3) were reported to be immunogenic. However, Conley exemplifies conjugates prepared using only a single carrier protein, OMPC. As discussed more fully below, the capping reaction itself may be disruptive to the carrier's ability to induce an immune response against the conjugated peptide immunogen. *See* paragraph 0008 of the specification (WO 2005/058940). Thus, even if a skilled artisan recognized that unreacted crosslinking agents on the carrier may undergo unwanted reactions, as the Examiner states (p. 4, 1st paragraph of the OA), the immunogenicity results for the OMPC carrier exemplified in Conley would not have provided the skilled artisan with a reasonable expectation

that the carrier proteins recited in the presently claimed invention could be capped while preserving the functionality of the carriers such that they retain their ability to elicit the desired immune response against the peptide immunogen that would otherwise not occur without a carrier.

The Use of Capping Molecules and Preservation of the "Carrier Effect"

As discussed in the specification, a disadvantage of the conventional techniques for the generation of immunogenic conjugates is that the introduction of reactive sites into amino acid side chains of the carrier protein produces reactive sites that, if not neutralized, are free to undergo unwanted reactions *in vitro* (thereby adversely effecting the functionality or stability of the conjugate) or *in vivo* (thereby posing a potential risk of adverse events in persons immunized with the conjugates). *See* paragraph 0008 of the published international application. Although capping can be accomplished using various known chemical reactions, the use of capping reagents may disrupt the ability of the resulting conjugate to function as an immunogenic agent having the desired properties of the "carrier effect." *Id.* Thus, the presently claimed invention is addressed to the problem of providing an immunogenic conjugate comprising a specified carrier protein that has been capped to improve safety and stability, while also retaining the carrier protein's ability to elicit the desired immune response against the conjugated peptide immunogen that would otherwise not occur without a carrier.

The presently claimed invention is based, in part, on Applicant's discovery that a capping molecule can be used with the claimed carrier proteins to avoid unwanted side reactions that may detrimentally impact the stability or safety of an immunogenic conjugate, while also preserving the conjugate's ability to elicit a desired immune response against the attached peptide immunogen. Immunogenic conjugates comprising a peptide immunogen coupled to each of the claimed carrier proteins, and capped as recited in the presently claimed invention are exemplified in the specification at Examples 1, 2 and 9. The immunogenicity of conjugates comprising each of the recited carriers is demonstrated in Examples 6 and 9, confirming that the functionality of the carrier proteins is preserved and the desired immune response is elicited.

The Cited Art does Not Teach Capping & Preservation of the "Carrier Effect" in the Claimed Carriers

Mariotti does not discuss capping of unreacted functional groups. Thus, Mariotti provides no guidance to the skilled artisan regarding the presently claimed invention.

Similarly, Conley provides no guidance to the skilled artisan regarding the presently claimed carriers because Conley neither discusses nor exemplifies the use of CRM_{197}, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, or *Chlamydia pneumoniae* ORF T858 as a carrier protein. Conley exemplifies the use of only a single carrier protein, OMPC, in the preparation of a capped immunogenic conjugate. As mentioned above, the use of chemical capping reagents to inactivate the unreacted derivatized functional groups on the carrier protein may be disruptive to the functionality of the resulting immunogenic conjugate. Thus, the single exemplary carrier of Conley would not have provided the skilled artisan with a reasonable expectation that the carrier proteins recited in independent claim 384 could be capped while preserving the functionality of the carrier to elicit the desired immune response against the peptide immunogen, as claimed.

In view of the foregoing, Applicants submit that the presently claimed invention is patentable over the cited art. Accordingly, Applicants respectfully request withdrawal of this ground of rejection.

Claims 392 and 394-396

Claims 392 and 394-396 are rejected under 35 USC 103(a) as allegedly being unpatentable over **Mariotti**, *supra*, in view of **Conley**, *supra*.

Applicants respectfully traverse. Each of claims 392 and 394-396 depends directly or indirectly from independent claim 384, discussed above. Thus, each of these claims is patentable over the cited art for at least the same reasons discussed above. Accordingly, Applicants respectfully request withdrawal of this ground of rejection.

Claim 402

Claim 402 is rejected under 355 USC 103(a) as allegedly being unpatentable over **Mariotti**, *supra*, and **Conley**, *supra*, in view of **Joyce** *et al.*, *Carbohydrate Research*, 338:903-

922 (2003). The Examiner states that Joyce teaches N-acetylcysteamine capping in the preparation of an immunogen.

Applicants respectfully traverse. Claim 402 depends from independent claim 384, discussed above, and is patentable over the cited art for at least the same reasons.

Joyce provides nothing to address the deficiencies of Mariotti and Conley outlined above. Rather, Joyce discusses the preparation of polysaccharide-OMPC conjugates and the capping of residual maleimides with N-acytylcysteamine. *See* paragraph 4.11 bridging pp. 920-921. Joyce discusses the use of the same singular carrier protein (OMPC) discussed in Conley. Thus, Joyce provides no guidance to the skilled artisan regarding capping and preservation of the carrier effect in a conjugate comprising any one of the presently claimed carrier proteins.

In view of the foregoing, Applicants respectfully request withdrawal of this ground of rejection.

Obviousness-Type Double Patenting Rejections

Claims 384, 386, 387, 392, 394-396 and 402 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claim 398 of copending Application No. 10/583,503.

Without agreeing with the Examiner's position, Applicants will consider submitting a terminal disclaimer, if appropriate, to obviate this rejection upon an indication that the presently claimed invention is otherwise allowable.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-838-2045.

Respectfully submitted,

Lance A. Termes
Reg. No. 43,184

Customer No. 00826
ALSTON & BIRD LLP
Bank of America Plaza
101 South Tryon Street, Suite 4000
Charlotte, NC 28280-4000
Tel: Silicon Valley Office (650) 838-2000
Fax: Charlotte Office (704) 444-1111
LAT:mrc

LEGAL02/32411668v1